

## Defining the molecular mechanisms of somatic cell reprogramming

### Grant Award Details

Defining the molecular mechanisms of somatic cell reprogramming

**Grant Type:** Basic Biology I

**Grant Number:** RB1-01353

**Project Objective:** This project explores the molecular mechanisms of somatic cell reprogramming, specifically testing hypotheses related to the interactions of Oct4/Klf4/Sox2, beta catenin and Pitx2.

**Investigator:**

**Name:** Wange Lu

**Institution:** University of Southern California

**Type:** PI

**Human Stem Cell Use:** iPS Cell

**Cell Line Generation:** iPS Cell

**Award Value:** \$1,365,580

**Status:** Closed

### Progress Reports

**Reporting Period:** Year 1

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**Reporting Period:** Year 2

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**Reporting Period:** Year 3 + NCE

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### Grant Application Details

**Application Title:** Defining the molecular mechanisms of somatic cell reprogramming

**Public Abstract:** The development of methods to "reprogram" adult cells such as skin cells by simultaneously expressing four specific factors — Oct3/4, Sox2, c-Myc and Klf4 — in order to create cells resembling embryonic stem (ES) cells is a major breakthrough in stem cell biology. Our ability to generate these cells, which are known as induced pluripotent stem (iPS) cells, will allow us to obtain stem cells capable of maturing into any tissue type, which is critical for research and has great therapeutic potential, without the controversial use of embryos. We envision that human iPS cells generated from a patient could be used to generate specific cells or tissues for cell replacement therapies for that individual patient, without stimulating an adverse immune response. Certain disease-specific iPS cells could also be differentiated into diseased tissues to study the causes of those diseases or to screen for drugs to treat them. Differentiated cells from iPS cells could also be used for toxicology tests before a drug is given to patients. Therefore, iPS cell technology may make individualized medicine a reality in the future. However, molecular changes that underlie reprogramming of body cells are not yet well understood and must be defined before iPS cells can be safely used for patient-specific therapy.

In this study we will undertake biochemical and molecular analysis to try to understand cellular changes mediating reprogramming. These studies should help us to develop novel strategies to make reprogramming more efficient so that iPS cells can be generated on a large scale for use in regenerative medicine, individualized medicine and drug discovery.

**Statement of Benefit to California:** California is the most populated state in the US. Many diseases and injuries suffered by the citizens of California, such as Alzheimer's and Parkinson's diseases, amyotrophic lateral sclerosis, multiple sclerosis, diabetes and cancer, could be treated using stem cells. The recent development of technology to transform skin cells into induced pluripotent stem (iPS) cells moves us one step closer to developing stem cells suitable for use as therapeutics. Stem cells generated from a patient could potentially be used to replace that individual's diseased or damaged tissues without concern about an immune response. Disease-specific iPS cells may also be used for drug discovery and toxicology studies. Defining mechanisms underlying iPS cell induction is important before iPS cells can be used for therapy to treat degenerative disease and injuries. This application aims to study molecular mechanisms of iPS cell induction. The knowledge gained from this study can help us improve the efficiency of iPS cell induction. Our findings could also be commercialized by California-based biotechnology companies to generate revenue and create new job opportunities, while at the same time addressing some of the most devastating healthcare issues in our state.

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